**Study Design**

This is a Phase 1a/2 study (NCT02330032) designed to evaluate safety, tolerability and pharmacokinetics (PK) following increasing doses of RX-5902. Primary objectives include evaluating safety, tolerability and dose limiting toxicities to identify the maximum tolerated dose and a recommended phase 2 dose (RP2D) and schedule (RPSD). Secondary objectives include evaluation of antitumor activity and antitumor activity (RESET at 1:1). Eligible subjects (aged ≥18 years) with relapsed/refractory solid tumors that had been heavily pretreated, received oral RX-5902 ranging from 25 mg to 350 mg and administered at 1, 3, 5 or 7 times per week for 3 weeks followed by 1 week of rest or for 4 weeks without rest.

**RESULTS:**

As of May 17, 2015, 35 subjects (22 Females, 13 males) were treated with oral RX-5902. The dose limiting toxicities were Grade 4 neutropenia (n=1) and Grade 2 fatigue (n=1) at 300 mg administered daily for 4 weeks. The maximum tolerated dose of 250 mg was determined at 4 weeks as shown in Table 2. The 250 mg dose was selected for further study. The adverse events were Grade 1, vomiting, diarrhea, weight loss and fatigue. Oral RX-5902 was bioavailable with median Tmax of 2 hours and median elimination half-life of 12 hours. The dose finding portion of the Phase 1 study (NCT02003092) was designed to evaluate safety, tolerability and dose limiting toxicities, to identify the maximum tolerated dose and a recommended phase 2 dose and schedule (RP2D). Secondary objectives were pharmacokinetics (PK) and antitumor activity (RESET at 1:1). Eligible subjects (aged ≥ 18 years), with relapsed/refractory solid tumors who receive oral RX-5902 for 1, 3, 5 or 7 times per week for 3 weeks followed by 1 week of rest or for 4 weeks without rest.

**CONCLUSIONS:**

The dose finding portion of the Phase 1 study (NCT02003092) was designed to evaluate safety, tolerability and dose limiting toxicities, to identify the maximum tolerated dose and a recommended phase 2 dose and schedule (RP2D). Secondary objectives include evaluation of antitumor activity and antitumor activity (RESET at 1:1). Eligible subjects (aged ≥18 years) with relapsed/refractory solid tumors who receive oral RX-5902 for 1, 3, 5 or 7 times per week for 3 weeks followed by 1 week of rest or for 4 weeks without rest.

**Pharmacokinetics**

Pharmacokinetic (PK) samples were collected on Day 1 (for single weekly dosing) and Day 15 (for multiple weekly doses) for at least 8 hours. A Population PK model was built and used for pharmacokinetic/pharmacodynamic assessments. There is a trend towards dose proportionality for the lower dose groups of the doses. The drug is absorbed orally modestly rapidly without a great deal of variability in Tmax. The PK parameters are shown in Table 3.

**Safety Profile**

Most frequent adverse events and their related adverse events are shown in Table 4. The most common adverse events were nausea, vomiting, diarrhea, headache, and vomiting. The number of adverse events was highest at 300 mg/day and lowest at 25 mg/day.

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**Conclusions**

- Early anti-tumor activity was observed in patients with breast (including triple negative), ovarian, neuroendocrine, paraganglioma, colorectal, cervical, squamous cell, and pancreatic cancers.
- There is a trend towards dose proportionality despite the low number of subjects at some of the doses.
- The recommended phase 2 dose is 250 mg/day for 5 consecutive days with 2 days of off for 4 weeks per cycle.
- The Phase 2 portion of the study targeting triple negative breast cancer or ovarian cancer is ongoing.

**Investigator Disclosures**

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For further information about RX-5902 and Rexahn Pharmaceuticals please contact Ely Benaim, benaim@rexahn.com (410) 365-3500 X542